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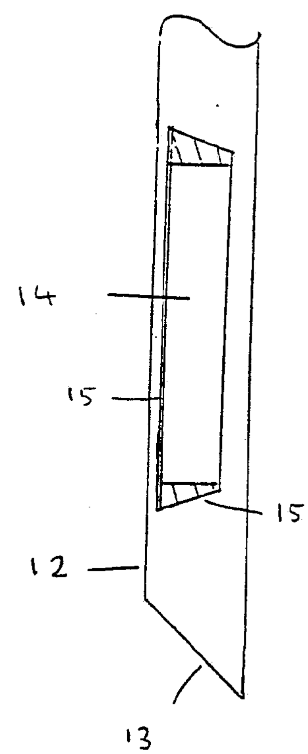
(54) Title: BLOOD GLUCOSE MONITORING

(57) Abstract

Apparatus for blood glucose monitoring, which comprises: (a) a total internal reflection waveguide having a core and reflective cladding, at least part of the core being devoid of such cladding; (b) a light source (such as a laser) optically coupled to an end of the waveguide; (c) a light detector arranged to generate a signal representing the quantity of light transmitted from the light source through the waveguide past the unclad part; and (d) an insulin administration device which is such that insulin is administered to a patient when the quantity of light detected by the detector changes by more than a predetermined amount.



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Blood Glucose Monitoring

The present invention is concerned with an apparatus and method for monitoring blood glucose, in which the refractive index of the blood is monitored or measured.

It is known to measure and indicate or record the refractive index of various liquids by detecting the attenuation of internally reflected light passing through a transparent optical waveguide, such as a glass rod, an optical fibre or the like.

Optical fibres generally have a central core, entirely surrounded by a plastics or glass sheath (the cladding). In order for optical transmission along such a fibre to take place, the refractive index of the core must be greater than that of the cladding. It is well known that the relative index of refraction of the core and cladding will determine the transmission characteristics of light along the optical fibre.

According to Snell's law, n_2 sin x n1 sin y, in which n1 is the refractive index of the cladding, n2 is the refractive index of the core, x is the angle of incidence at the core/cladding interface and y is the angle at which an optical beam transmitted along the core escapes therefrom. If n_1 and n_2 remain constant, then there is an angle x at which y will equal 90 degrees; this angle (called the critical angle) is the minimum angle at which total internal reflection takes place.

If a ray of light strikes the core/cladding interface at an angle greater than the critical angle, then the ray will be internally reflected within the core at a reflected angle equal to the angle of incidence; if the angle of incidence is less than the critical angle, then losses will occur. The critical angle (Xcr) is derived from Snell's law as Xcr = arc sin (n_1/n_2).

If part of the cladding is removed, then the degree of attenuation of a light beam transmitted along the optical fibre will depend on the refractive index of the medium in which the bared portion of optical fibre or other waveguide is disposed. This phenomenon has been proposed as the basis for measurement of the refractive index of a test liquid in, for example, U.K. patent specifications 2105034 and 1507747.

We have now established that this type of technique is particularly suitable for producing a measure of glucose concentration in blood, because variation in the glucose concentration causes detectable variation in the refractive index.

The blood glucose concentration of a healthy person is generally about 1% (by weight), although a variation of plus or minus 0.3% is acceptable. In a diabetic patient, the blood glucose concentration can vary widely, which can result in serious complications, such as cardiovascular problems and eye disorders. We have established that a 0.1% change in glucose concentration can result in a change of the optical transmission of greater than 1%, which is a substantial and detectable change.

A blood glucose monitor which measures the glucose level of blood using a refractometer is known from U.S. Patent 4704029. In the blood glucose monitor disclosed in the latter document, a prism is used to form an optical interface with the blood being monitored.

We have found that the use of such a prism requires a bulky insert into the body of the patient; furthermore, a rigid support is required for the prism to prevent movement which could otherwise cause irregularities in the detected refractive index. It is an object of the present invention to provide blood glucose monitoring apparatus in which the above disadvantages are at least alleviated.

According to the present invention, therefore, there is provided apparatus for monitoring the glucose level of blood which comprises an elongate optical waveguide capable of transmitting light by internal reflection, said waveguide comprising a core and a reflective cladding, at least part of the core being devoid of said cladding, said part being such that it can be positioned in direct contact with the blood to be monitored; a light source (such as a laser) optically coupled to an end of the optical waveguide; light detection means arranged to generate a signal representative of the quantity of light transmitted from the light source through the waveguide via said part; and means for initiating insulin administration when the quantity of light detected by said light detection means changes by more than a predetermined amount.

The present invention further comprises a method of determining the glucose content of blood, which comprises transmitting a light beam along an optical waveguide, in which at least one portion of the waveguide is devoid of reflective cladding and is in contact with the blood; and monitoring the attenuation of transmitted light passing said unclad portion. The output from the optical waveguide is preferably used to provide positive feedback control of administration of insulin to a patient. The method according to the invention is preferably carried out using apparatus according to the invention.

The light detection means may, in one embodiment of the invention, be coupled to an output end of the waveguide remote from the light source end. However, this may necessitate the location of processing electronics at the output end; according to another embodiment of the invention, therefore, the waveguide may be provided with a reflective end remote from the light source. In this case, the light detection means is coupled to an output end of the waveguide remote from the reflective end.

In a preferred embodiment of the invention, a further optical waveguide is provided in thermal contact with the first-mentioned optical waveguide along substantially the entire length of the unclad portion. This further optical waveguide is preferably clad along substantially its entire length, such that there is substantially minimal optical attenuation along the length thereof. This further optical waveguide thus provides compensation for extraneous changes in refractive index (such as those caused by temperature changes).

The optical waveguide used in the method and apparatus according to the invention may be a conventional optical fibre; optical fibres generally have a good quality, consistent circular cross-section. According to a preferred embodiment of the invention, however, the optical waveguide preferably comprises an elongate body with a polygonal (e.g. rectangular) cross-section, preferably with geometrically parallel faces along the length of the waveguide. The use of a waveguide with such parallel faces substantially minimises distortion and loss of clarity of the transmitted optical beam. The flat surfaces of the rectangular cross-section may advantageously be polished to optical quality.

The invention will be further described, by way of example only, with reference to the accompanying drawings, in which:

Figure 1 is a schematic illustration of glucose monitoring apparatus according to the invention; and

Figure 2 is a sectional view of apparatus for injecting a waveguide into a patient's bloodstream, for use in apparatus according to the invention.

Referring to Figure 1 there is shown a blood flow 1 in the direction of arrow A along tubular member 11 (which may be a blood vessel or an extracorporeal conduit); an optical waveguide 2, an unclad portion of which is diposed in the blood flow. Part of the output from a laser source 3 is passed to a reference photodiode 4 and the remainder of the output to a signal photodiode 5. The outputs from both reference photodiode 4 and signal photodiode 5 are passed to electronic signal processor 6. The output from the processor is then input to an analogue-to-digital convertor 7, the digital output of which is input to a process controller 8 (e.g. a single chip microprocessor). The process controller is operatively connected to an insulin pump 9, arranged for administration of insulin 10 to the blood flow 1.

The processed signal from photodiode 5 is compared by signal processor 6 with that from reference photodiode 4, so as to give a measure of the attenuation of light through the waveguide 2. The resultant measure of attenuation of light can, when the system is appropriately calibrated, give a measure of the refractive index of the blood and therefore the glucose content thereof; the signal processor 6 is used to generate a signal which is itself arranged to trigger operation of the insulin pump 9 and thence administration of insulin into the blood.

In a preferred embodiment of the invention, the part of the output from the laser source 3 which is passed to reference photodiode 4 may pass in parallel to the light passed

through the waveguide 2 through a further waveguide (not shown) which is in thermal contact with waveguide 2 preferably along the entire length thereof.

Referring to Figure 2, there is shown a hollow jacket 12 having a sharp pointed end 13 to be inserted into a patient by means of a hypodermic injection device (not shown). Located within the jacket is the free end portion of a waveguide 14 having a reflective end 15 and a portion 16 with the cladding removed.

In use, the pointed end 13 of jacket 12 is inserted into a blood vessel of a patient; the jacket is then removed leaving the waveguide in place. A light source and detector electronics are then coupled to the external end of the waveguide, which can then be used to control the administration of insulin to the patient.

CLAIMS:

1. Apparatus for monitoring the glucose content of blood, which comprises an elongate optical waveguide capable of transmitting light by internal reflection, said waveguide comprising a core and a reflective cladding, at least part of the core being devoid of said cladding, said part being such that it can be positioned in direct contact with the blood to be monitored; a light source optically coupled to an end of the optical waveguide; light detection means arranged to generate a signal representative of the quantity of light transmitted from the light source through the waveguide via said part; and means for initiating insulin administration to said blood when the quantity of light detected by the detector changes by more than a predetermined amount.

2. Apparatus according to claim 1, wherein said light source is a laser.

3. Apparatus according to claim 1 or 2, which further comprises means for insertion of at least the unclad portion of said waveguide into the bloodstream of a patient.

4. Apparatus according to claim 3, wherein said insertion means comprises a sharp metal housing arranged to be secured to a hypodermic syringe or the like, said housing substantially encompassing said unclad portion.

5. Apparatus according to any of claims 1 to 4, wherein said light detection means is coupled to an output end of said waveguide remote from said light source end.

6. Apparatus according to any of claims 1 to 4, wherein said waveguide is provided with a reflective end remote from said light source end, said light detection means being coupled to an output end of said waveguide remote from said reflective end.

7. Apparatus according to any of claims 1 to 6, wherein a further optical waveguide is provided in thermal contact with said first-mentioned optical waveguide along substantially the entire length of the unclad portion thereof, preferably along substantially the entire length of the first-mentioned waveguide.

8. Apparatus according to any of claims 1 to 7, wherein said optical waveguide comprises an elongate body having a polygonal cross-section.

9. A method of determining the glucose content of blood, which comprises transmitting a light beam along an optical waveguide, in which at least one portion of the waveguide is devoid of reflective cladding and is in contact with said blood; monitoring the attenuation of transmitted light passing said unclad portion; and, preferably, using the output from the optical waveguide to provide positive feedback control of administration of insulin to a patient.

10. A method according to claim 9, wherein apparatus according to any of claims 1 to 8 is employed.

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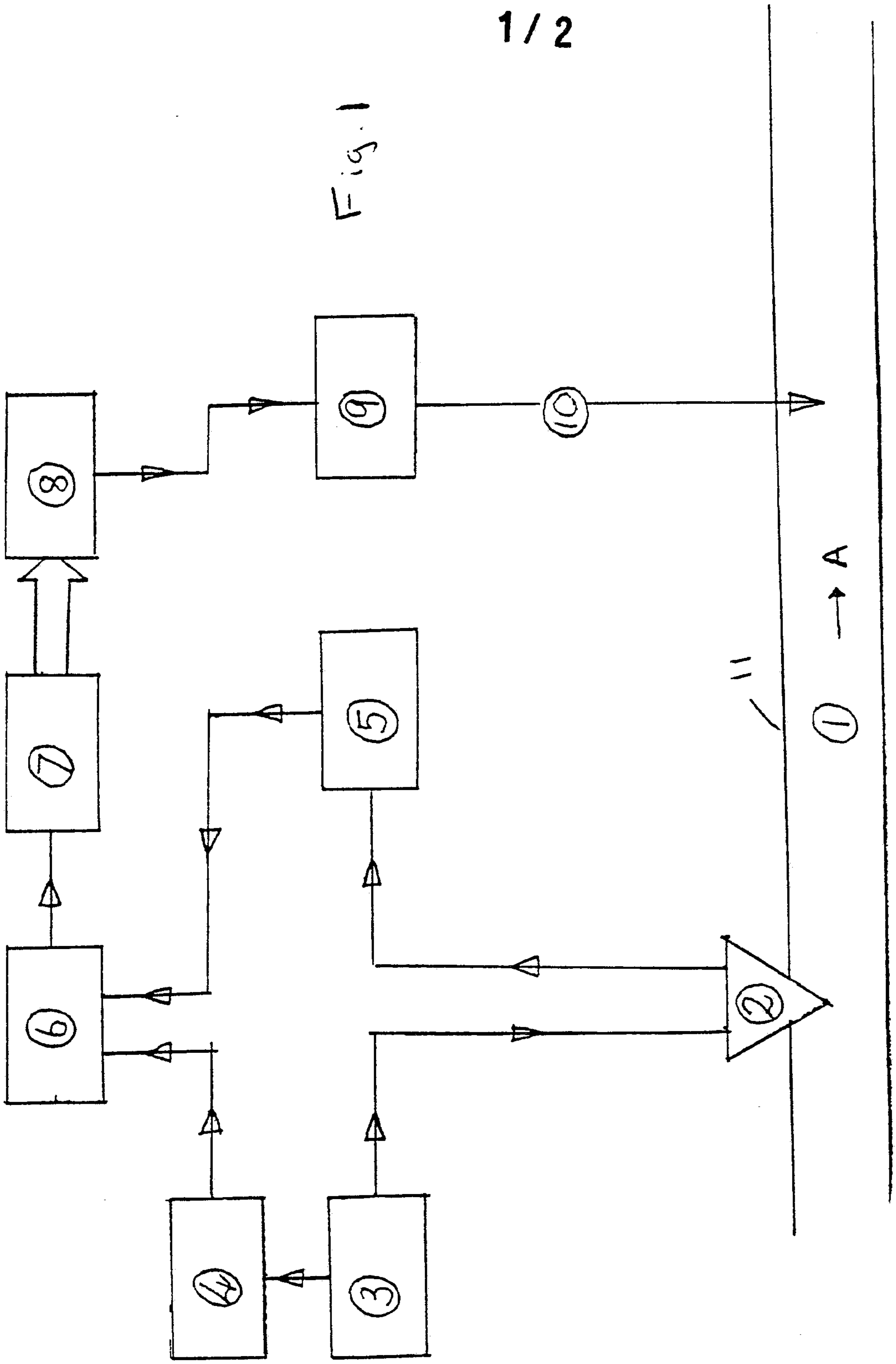

Fig. 1

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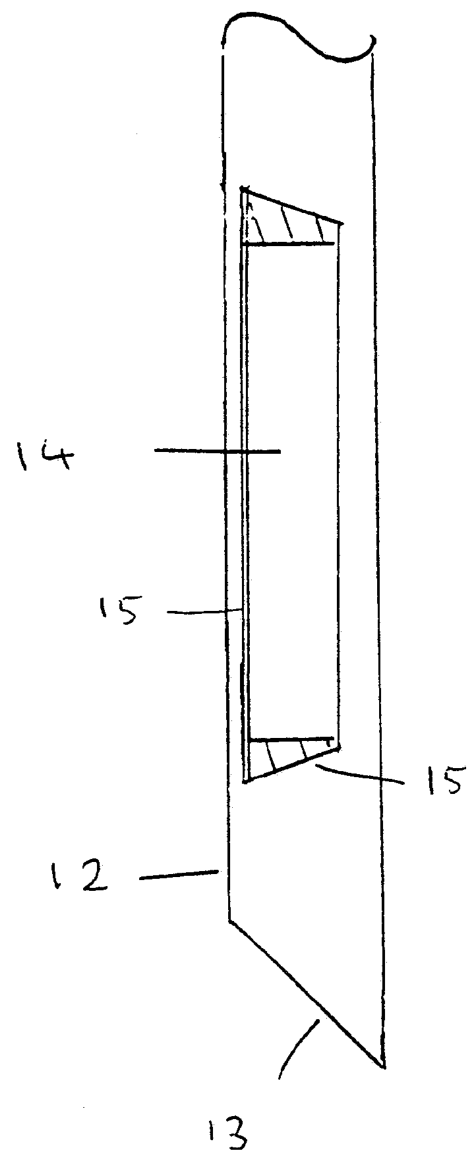

Fig. 2

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 89/00899

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC
IPC4: G 01 N 33/48, 21/55; A 61 B 5/14

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC4	G 01 N; A 61 B

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
Y	Optics and Laser Technology, Vol. 17, No. 1, February 1985, I.N. Ross et al.: "Optical monitoring of glucose concentration ", see pages 31-35 see in particular fig. 8 and the abstract --	1-10
Y	US, A, 4 706 677 (M. S. GORKY ET AL.) 17 November 1987, see the whole document --	1-10
Y	WO, A1, 88/01376 (RADIOMETER A/S) 25 February 1988, see claims 1, 8 and 17 and pages 1-8, page 9 line 30 and page 11, lines 6-16	1,5,8
X	 --	9

* Special categories of cited documents: [10]

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
27th October 1989	15. 01. 90
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	T.K. WILLIS

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

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ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. PCT/GB 89/00899

SA 30497

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on 14/09/89
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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82